

## APPENDIX A. ATSDR MINIMAL RISK LEVELS AND WORKSHEETS

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99–499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of

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the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as 100-fold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology and Environmental Medicine, expert panel peer reviews, and agency-wide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology and Environmental Medicine, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road NE, Mailstop F-32, Atlanta, Georgia 30333.

For reasons discussed in Section 2.3, MRLs were not derived for radon.

## APPENDIX B. USER'S GUIDE

### Chapter 1

#### Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public, especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

### Chapter 2

#### Relevance to Public Health

This chapter provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions:

1. What effects are known to occur in humans?
2. What effects observed in animals are likely to be of concern to humans?
3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The chapter covers end points in the same order that they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, and dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). *In vitro* data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this chapter.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal Risk Levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Chapter 3 Data Needs section.

#### Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, ATSDR has derived MRLs for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action, but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans.

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MRLs should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2, "Relevance to Public Health," contains basic information known about the substance. Other sections such as Chapter 3 Section 3.9, "Interactions with Other Substances," and Section 3.10, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology that the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses (RfDs) for lifetime exposure.

To derive an MRL, ATSDR generally selects the most sensitive end point which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen end point are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest no-observed-adverse-effect level (NOAEL) that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the levels of significant exposure (LSE) tables.

## **Chapter 3**

### **Health Effects**

#### **Tables and Figures for Levels of Significant Exposure (LSE)**

Tables and figures are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, MRLs to humans for noncancer end points, and EPA's estimated range associated with an upper-bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of NOAELs, LOAELs, or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 3-1 and Figure 3-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

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**LEGEND****See Sample LSE Table 3-1 (page B-6)**

- (1) **Route of Exposure.** One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. Typically when sufficient data exist, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Tables 3-1, 3-2, and 3-3, respectively). LSE figures are limited to the inhalation (LSE Figure 3-1) and oral (LSE Figure 3-2) routes. Not all substances will have data on each route of exposure and will not, therefore, have all five of the tables and figures.
- (2) **Exposure Period.** Three exposure periods—acute (less than 15 days), intermediate (15–364 days), and chronic (365 days or more)—are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.
- (3) **Health Effect.** The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).
- (4) **Key to Figure.** Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the two "18r" data points in sample Figure 3-1).
- (5) **Species.** The test species, whether animal or human, are identified in this column. Chapter 2, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 3.4, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.
- (6) **Exposure Frequency/Duration.** The duration of the study and the weekly and daily exposure regimens are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to "Chemical x" via inhalation for 6 hours/day, 5 days/week, for 13 weeks. For a more complete review of the dosing regimen, refer to the appropriate sections of the text or the original reference paper (i.e., Nitschke et al. 1981).
- (7) **System.** This column further defines the systemic effects. These systems include respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, one systemic effect (respiratory) was investigated.
- (8) **NOAEL.** A NOAEL is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system, which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

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- (9) LOAEL. A LOAEL is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific end point used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less Serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.
- (10) Reference. The complete reference citation is given in Chapter 9 of the profile.
- (11) CEL. A CEL is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.
- (12) Footnotes. Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates that the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

**LEGEND****See Sample Figure 3-1 (page B-7)**

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

- (13) Exposure Period. The same exposure periods appear as in the LSE table. In this example, health effects observed within the acute and intermediate exposure periods are illustrated.
- (14) Health Effect. These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.
- (15) Levels of Exposure. Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m<sup>3</sup> or ppm and oral exposure is reported in mg/kg/day.
- (16) NOAEL. In this example, the open circle designated 18r identifies a NOAEL critical end point in the rat upon which an intermediate inhalation exposure MRL is based. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).
- (17) CEL. Key number 38m is one of three studies for which CELs were derived. The diamond symbol refers to a CEL for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

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- (18) Estimated Upper-Bound Human Cancer Risk Levels. This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA's Human Health Assessment Group's upper-bound estimates of the slope of the cancer dose response curve at low dose levels ( $q_1^*$ ).
- (19) Key to LSE Figure. The Key explains the abbreviations and symbols used in the figure.

**SAMPLE**

1 →

**Table 3-1. Levels of Significant Exposure to [Chemical x] – Inhalation**

| Key to figure <sup>a</sup>   | Species  | Exposure frequency/<br>duration | System                        | NOAEL (ppm) | LOAEL (effect)     |   | Reference            |
|------------------------------|----------|---------------------------------|-------------------------------|-------------|--------------------|---|----------------------|
|                              |          |                                 |                               |             | Less serious (ppm) | Serious (ppm)                           |                      |
| <b>INTERMEDIATE EXPOSURE</b> |          |                                 |                               |             |                    |   |                      |
|                              | 5        | 6                               | 7                             | 8           | 9                  |   | 10                   |
| 3 →                          | Systemic | ↓                               | ↓                             | ↓           | ↓                  | ↓                                       | ↓                    |
| 4 →                          | 18       | Rat                             | 13 wk<br>5 d/wk<br>6 hr/d     | Resp        | 3 <sup>b</sup>     | 10 (hyperplasia)                        | Nitschke et al. 1981 |
| <b>CHRONIC EXPOSURE</b>      |          |                                 |                               |             |                    |   |                      |
|                              | Cancer   |                                 |                               |             |                    | 11                                      |                      |
|                              |          |                                 |                               |             | ↓                  |   |                      |
|                              | 38       | Rat                             | 18 mo<br>5 d/wk<br>7 hr/d     |             |                    | 20 (CEL, multiple organs)               | Wong et al. 1982     |
|                              | 39       | Rat                             | 89–104 wk<br>5 d/wk<br>6 hr/d |             |                    | 10 (CEL, lung tumors, nasal tumors)     | NTP 1982             |
|                              | 40       | Mouse                           | 79–103 wk<br>5 d/wk<br>6 hr/d |             |                    | 10 (CEL, lung tumors, hemangiosarcomas) | NTP 1982             |

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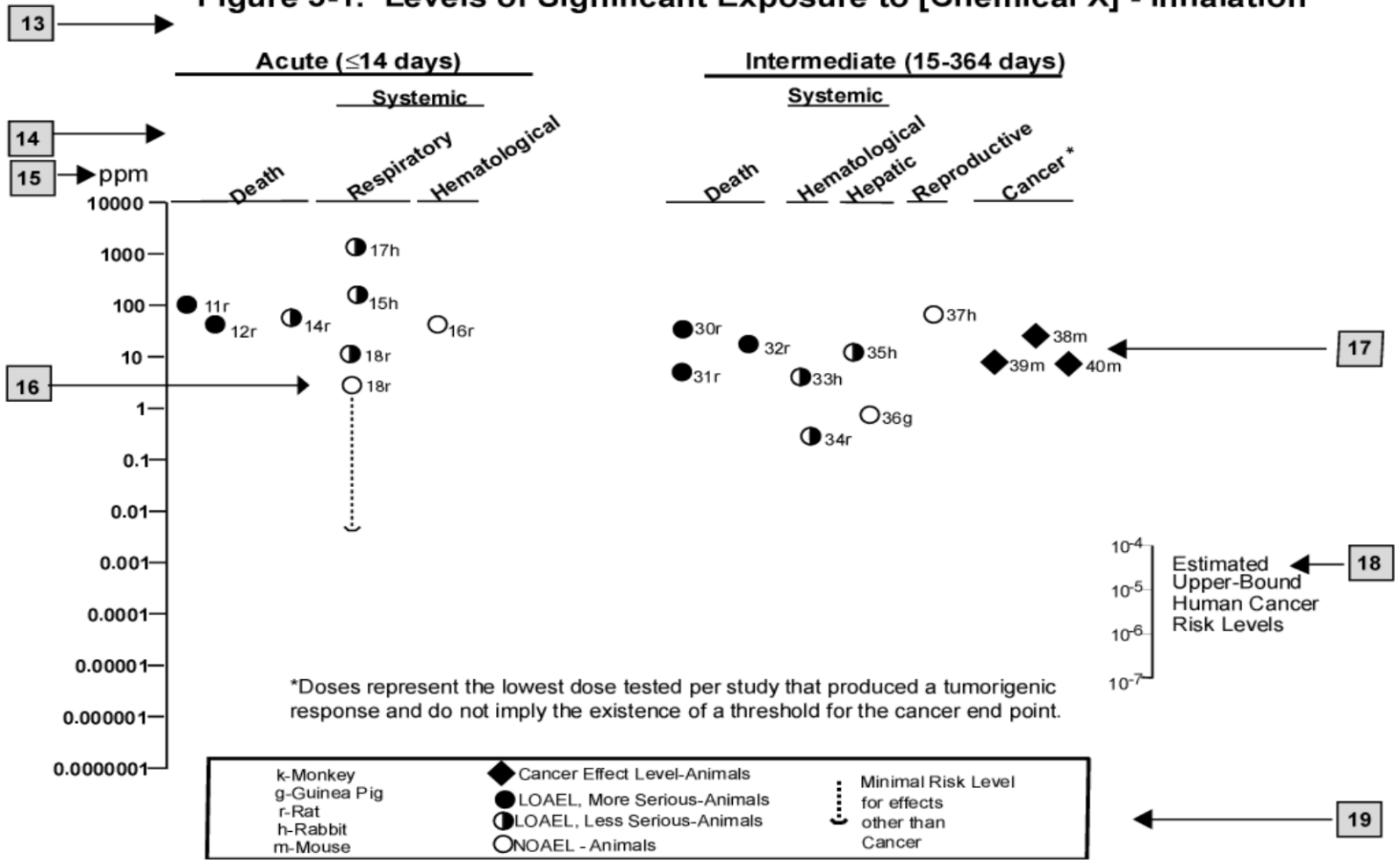
<sup>a</sup> The number corresponds to entries in Figure 3-1.

<sup>b</sup> Used to derive an intermediate inhalation Minimal Risk Level (MRL) of  $5 \times 10^{-3}$  ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).



# SAMPLE

### Figure 3-1. Levels of Significant Exposure to [Chemical X] - Inhalation



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## APPENDIX C. ACRONYMS, ABBREVIATIONS, AND SYMBOLS

|                   |   |
|-------------------|---|
| ACGIH             | American Conference of Governmental Industrial Hygienists             |
| ACOEM             | American College of Occupational and Environmental Medicine           |
| ADI               | acceptable daily intake   |
| ADME              | absorption, distribution, metabolism, and excretion                   |
| AED               | atomic emission detection   |
| AFID              | alkali flame ionization detector                                      |
| AFOSH             | Air Force Office of Safety and Health                                 |
| ALT               | alanine aminotransferase  |
| AML               | acute myeloid leukemia  |
| AOAC              | Association of Official Analytical Chemists                           |
| AOEC              | Association of Occupational and Environmental Clinics                 |
| AP                | alkaline phosphatase  |
| APHA              | American Public Health Association                                    |
| AST               | aspartate aminotransferase  |
| atm               | atmosphere  |
| ATSDR             | Agency for Toxic Substances and Disease Registry                      |
| AWQC              | Ambient Water Quality Criteria  |
| BAT               | best available technology   |
| BCF               | bioconcentration factor   |
| BEI               | Biological Exposure Index   |
| BMD               | benchmark dose  |
| BMD/C             | benchmark dose or benchmark concentration                             |
| BMD <sub>x</sub>  | dose that produces a X% change in response rate of an adverse effect  |
| BMDL <sub>x</sub> | 95% lower confidence limit on the BMD <sub>x</sub>                    |
| BMDs              | Benchmark Dose Software   |
| BSC               | Board of Scientific Counselors  |
| C                 | centigrade  |
| CAA               | Clean Air Act   |
| CAG               | Cancer Assessment Group of the U.S. Environmental Protection Agency   |
| CAS               | Chemical Abstract Services  |
| CDC               | Centers for Disease Control and Prevention                            |
| CEL               | cancer effect level   |
| CELDS             | Computer-Environmental Legislative Data System                        |
| CERCLA            | Comprehensive Environmental Response, Compensation, and Liability Act |
| CFR               | Code of Federal Regulations   |
| Ci                | curie   |
| CI                | confidence interval   |
| CL                | ceiling limit value   |
| CLP               | Contract Laboratory Program   |
| cm                | centimeter  |
| CML               | chronic myeloid leukemia  |
| CPSC              | Consumer Products Safety Commission                                   |
| CWA               | Clean Water Act   |
| DHEW              | Department of Health, Education, and Welfare                          |
| DHHS              | Department of Health and Human Services                               |
| DNA               | deoxyribonucleic acid   |
| DOD               | Department of Defense   |
| DOE               | Department of Energy  |
| DOL               | Department of Labor   |

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|                    |   |
|--------------------|---|
| DOT                | Department of Transportation  |
| DOT/UN/<br>NA/IMDG | Department of Transportation/United Nations/<br>North America/Intergovernmental Maritime Dangerous Goods Code |
| DWEL               | drinking water exposure level   |
| ECD                | electron capture detection  |
| ECG/EKG            | electrocardiogram   |
| EEG                | electroencephalogram  |
| EEGL               | Emergency Exposure Guidance Level   |
| EPA                | Environmental Protection Agency   |
| F                  | Fahrenheit  |
| F <sub>1</sub>     | first-filial generation   |
| FAO                | Food and Agricultural Organization of the United Nations  |
| FDA                | Food and Drug Administration  |
| FEMA               | Federal Emergency Management Agency   |
| FIFRA              | Federal Insecticide, Fungicide, and Rodenticide Act   |
| FPD                | flame photometric detection   |
| fpm                | feet per minute   |
| FR                 | Federal Register  |
| FSH                | follicle stimulating hormone  |
| g                  | gram  |
| GC                 | gas chromatography  |
| gd                 | gestational day   |
| GLC                | gas liquid chromatography   |
| GPC                | gel permeation chromatography   |
| HPLC               | high-performance liquid chromatography  |
| HRGC               | high resolution gas chromatography  |
| HSDB               | Hazardous Substance Data Bank   |
| IARC               | International Agency for Research on Cancer   |
| IDLH               | immediately dangerous to life and health  |
| ILO                | International Labor Organization  |
| IRIS               | Integrated Risk Information System  |
| K <sub>d</sub>     | adsorption ratio  |
| kg                 | kilogram  |
| kkg                | metric ton  |
| K <sub>oc</sub>    | organic carbon partition coefficient  |
| K <sub>ow</sub>    | octanol-water partition coefficient   |
| L                  | liter   |
| LC                 | liquid chromatography   |
| LC <sub>50</sub>   | lethal concentration, 50% kill  |
| LC <sub>Lo</sub>   | lethal concentration, low   |
| LD <sub>50</sub>   | lethal dose, 50% kill   |
| LD <sub>Lo</sub>   | lethal dose, low  |
| LDH                | lactic dehydrogenase  |
| LH                 | lutinizing hormone  |
| LOAEL              | lowest-observed-adverse-effect level  |
| LSE                | Levels of Significant Exposure  |
| LT <sub>50</sub>   | lethal time, 50% kill   |
| m                  | meter   |
| MA                 | <i>trans,trans</i> -muconic acid  |
| MAL                | maximum allowable level   |
| mCi                | millicurie  |

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|          |  |
|----------|--|
| MCL      | maximum contaminant level                                    |
| MCLG     | maximum contaminant level goal                               |
| MF       | modifying factor   |
| MFO      | mixed function oxidase                                       |
| mg       | milligram  |
| mL       | milliliter   |
| mm       | millimeter   |
| mmHg     | millimeters of mercury                                       |
| mmol     | millimole  |
| mppcf    | millions of particles per cubic foot                         |
| MRL      | Minimal Risk Level   |
| MS       | mass spectrometry  |
| NAAQS    | National Ambient Air Quality Standard                        |
| NAS      | National Academy of Science                                  |
| NATICH   | National Air Toxics Information Clearinghouse                |
| NATO     | North Atlantic Treaty Organization                           |
| NCE      | normochromatic erythrocytes                                  |
| NCEH     | National Center for Environmental Health                     |
| NCI      | National Cancer Institute                                    |
| ND       | not detected   |
| NFPA     | National Fire Protection Association                         |
| ng       | nanogram   |
| NHANES   | National Health and Nutrition Examination Survey             |
| NIEHS    | National Institute of Environmental Health Sciences          |
| NIOSH    | National Institute for Occupational Safety and Health        |
| NIOSHTIC | NIOSH's Computerized Information Retrieval System            |
| NLM      | National Library of Medicine                                 |
| nm       | nanometer  |
| nmol     | nanomole   |
| NOAEL    | no-observed-adverse-effect level                             |
| NOES     | National Occupational Exposure Survey                        |
| NOHS     | National Occupational Hazard Survey                          |
| NPD      | nitrogen phosphorus detection                                |
| NPDES    | National Pollutant Discharge Elimination System              |
| NPL      | National Priorities List                                     |
| NR       | not reported   |
| NRC      | National Research Council                                    |
| NS       | not specified  |
| NSPS     | New Source Performance Standards                             |
| NTIS     | National Technical Information Service                       |
| NTP      | National Toxicology Program                                  |
| ODW      | Office of Drinking Water, EPA                                |
| OERR     | Office of Emergency and Remedial Response, EPA               |
| OHM/TADS | Oil and Hazardous Materials/Technical Assistance Data System |
| OPP      | Office of Pesticide Programs, EPA                            |
| OPPT     | Office of Pollution Prevention and Toxics, EPA               |
| OPPTS    | Office of Prevention, Pesticides and Toxic Substances, EPA   |
| OR       | odds ratio   |
| OSHA     | Occupational Safety and Health Administration                |
| OSW      | Office of Solid Waste, EPA                                   |
| OTS      | Office of Toxic Substances                                   |

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|                  |  |
|------------------|--|
| OW               | Office of Water                                  |
| OWRS             | Office of Water Regulations and Standards, EPA   |
| PAH              | polycyclic aromatic hydrocarbon                  |
| PBPD             | physiologically based pharmacodynamic            |
| PBPK             | physiologically based pharmacokinetic            |
| PCE              | polychromatic erythrocytes                       |
| PEL              | permissible exposure limit                       |
| pg               | picogram   |
| PHS              | Public Health Service                            |
| PID              | photo ionization detector                        |
| pmol             | picomole   |
| PMR              | proportionate mortality ratio                    |
| ppb              | parts per billion                                |
| ppm              | parts per million                                |
| ppt              | parts per trillion                               |
| PSNS             | pretreatment standards for new sources           |
| RBC              | red blood cell                                   |
| REL              | recommended exposure level/limit                 |
| RfC              | reference concentration                          |
| RfD              | reference dose                                   |
| RNA              | ribonucleic acid                                 |
| RQ               | reportable quantity                              |
| RTECS            | Registry of Toxic Effects of Chemical Substances |
| SARA             | Superfund Amendments and Reauthorization Act     |
| SCE              | sister chromatid exchange                        |
| SGOT             | serum glutamic oxaloacetic transaminase          |
| SGPT             | serum glutamic pyruvic transaminase              |
| SIC              | standard industrial classification               |
| SIM              | selected ion monitoring                          |
| SMCL             | secondary maximum contaminant level              |
| SMR              | standardized mortality ratio                     |
| SNARL            | suggested no adverse response level              |
| SPEGL            | Short-Term Public Emergency Guidance Level       |
| STEL             | short term exposure limit                        |
| STORET           | Storage and Retrieval                            |
| TD <sub>50</sub> | toxic dose, 50% specific toxic effect            |
| TLV              | threshold limit value                            |
| TOC              | total organic carbon                             |
| TPQ              | threshold planning quantity                      |
| TRI              | Toxics Release Inventory                         |
| TSCA             | Toxic Substances Control Act                     |
| TWA              | time-weighted average                            |
| UF               | uncertainty factor                               |
| U.S.             | United States                                    |
| USDA             | United States Department of Agriculture          |
| USGS             | United States Geological Survey                  |
| VOC              | volatile organic compound                        |
| WBC              | white blood cell                                 |
| WHO              | World Health Organization                        |

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|               |                          |
|---------------|--------------------------|
| >             | greater than             |
| $\geq$        | greater than or equal to |
| =             | equal to                 |
| <             | less than                |
| $\leq$        | less than or equal to    |
| %             | percent                  |
| $\alpha$      | alpha                    |
| $\beta$       | beta                     |
| $\gamma$      | gamma                    |
| $\delta$      | delta                    |
| $\mu\text{m}$ | micrometer               |
| $\mu\text{g}$ | microgram                |
| $q_1^*$       | cancer slope factor      |
| -             | negative                 |
| +             | positive                 |
| (+)           | weakly positive result   |
| (-)           | weakly negative result   |

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## APPENDIX D. OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY, AND BIOLOGY

Understanding the basic concepts in radiation physics, chemistry, and biology is important to the evaluation and interpretation of radiation-induced adverse health effects and to the derivation of radiation protection principles. This appendix presents a brief overview of the areas of radiation physics, chemistry, and biology and is based to a large extent on the reviews of Mettler and Moseley (1985), Hobbs and McClellan (1986), Eichholz (1982), Hendee (1973), Cember (1996), and Early et al. (1979).

### D.1 RADIONUCLIDES AND RADIOACTIVITY

The substances we call elements are composed of atoms. Atoms in turn are made up of neutrons, protons and electrons: neutrons and protons in the nucleus and electrons in a cloud of orbits around the nucleus. Nuclide is the general term referring to any nucleus along with its orbital electrons. The nuclide is characterized by the composition of its nucleus and hence by the number of protons and neutrons in the nucleus. All atoms of an element have the same number of protons (this is given by the atomic number) but may have different numbers of neutrons (this is reflected by the atomic mass numbers or atomic weight of the element). Atoms with different atomic mass but the same atomic numbers are referred to as isotopes of an element.

The numerical combination of protons and neutrons in most nuclides is such that the nucleus is quantum mechanically stable and the atom is said to be stable, i.e., not radioactive; however, if there are too few or too many neutrons, the nucleus is unstable and the atom is said to be radioactive. Unstable nuclides undergo radioactive transformation, a process in which a neutron or proton converts into the other and a beta particle is emitted, or else an alpha particle is emitted. Each type of decay is typically accompanied by the emission of gamma rays. These unstable atoms are called radionuclides; their emissions are called ionizing radiation; and the whole property is called radioactivity. Transformation or decay results in the formation of new nuclides some of which may themselves be radionuclides, while others are stable nuclides. This series of transformations is called the decay chain of the radionuclide. The first radionuclide in the chain is called the parent; the subsequent products of the transformation are called progeny, daughters, or decay products.

In general there are two classifications of radioactivity and radionuclides: natural and artificial (man-made). Naturally-occurring radioactive material (NORM) exists in nature and no additional energy is necessary to place them in an unstable state. Natural radioactivity is the property of some naturally occurring, usually heavy elements, that are heavier than lead. Radionuclides, such as radium and uranium, primarily emit alpha particles. Some lighter elements such as carbon-14 and tritium (hydrogen-3) primarily emit beta particles as they transform to a more stable atom. Natural radioactive atoms heavier than lead cannot attain a stable nucleus heavier than lead. Everyone is exposed to background radiation from naturally-occurring radionuclides throughout life. This background radiation is the major source of radiation exposure to man and arises from several sources. The natural background exposures are frequently used as a standard of comparison for exposures to various artificial sources of ionizing radiation.

Artificial radioactive atoms are produced either as a by-product of fission of uranium or plutonium atoms in a nuclear reactor or by bombarding stable atoms with particles, such as neutrons or protons, directed at the stable atoms with high velocity. These artificially produced radioactive elements usually decay by emission of particles, such as positive or negative beta particles and one or more high energy photons (gamma rays). Unstable (radioactive) atoms of any element can be produced.

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Both naturally occurring and artificial radioisotopes find application in medicine, industrial products, and consumer products. Some specific radioisotopes, called fall-out, are still found in the environment as a result of nuclear weapons use or testing.

## D.2 RADIOACTIVE DECAY

### D.2.1 Principles of Radioactive Decay

The stability of an atom is the result of the balance of the forces of the various components of the nucleus. An atom that is unstable (radionuclide) will release energy (decay) in various ways and transform to stable atoms or to other radioactive species called daughters, often with the release of ionizing radiation. If there are either too many or too few neutrons for a given number of protons, the resulting nucleus may undergo transformation. For some elements, a chain of daughter decay products may be produced until stable atoms are formed. Radionuclides can be characterized by the type and energy of the radiation emitted, the rate of decay, and the mode of decay. The mode of decay indicates how a parent compound undergoes transformation. Radiations considered here are primarily of nuclear origin, i.e., they arise from nuclear excitation, usually caused by the capture of charged or uncharged nucleons by a nucleus, or by the radioactive decay or transformation of an unstable nuclide. The type of radiation may be categorized as charged or uncharged particles, protons, and fission products) or electromagnetic radiation (gamma rays and x rays). Table D-1 summarizes the basic characteristics of the more common types of radiation encountered.

### D.2.2 Half-Life and Activity

For any given radionuclide, the rate of decay is a first-order process that is constant, regardless of the radioactive atoms present and is characteristic for each radionuclide. The process of decay is a series of random events; temperature, pressure, or chemical combinations do not effect the rate of decay. While it may not be possible to predict exactly which atom is going to undergo transformation at any given time, it is possible to predict, on average, the fraction of the radioactive atoms that will transform during any interval of time.

The *activity* is a measure of the quantity of radioactive material. For these radioactive materials it is customary to describe the activity as the number of disintegrations (transformations) per unit time. The unit of activity is the curie (Ci), which was originally related to the activity of one gram of radium, but is now defined as that quantity of radioactive material in which there are:

1 curie (Ci) =  $3.7 \times 10^{10}$  disintegrations (transformations)/second (dps) or  $2.22 \times 10^{12}$  disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = that quantity of radioactive material in which there is 1 transformation/second. Since activity is proportional to the number of atoms of the radioactive material, the quantity of any radioactive material is usually expressed in curies, regardless of its purity or concentration. The transformation of radioactive nuclei is a random process, and the number of transformations is directly proportional to the number of radioactive atoms present. For any pure radioactive substance, the rate of decay is usually described by its radiological half-life,  $T_R$ , i.e., the time it takes for a specified source material to decay to half its initial activity. The specific activity is an indirect measure of the rate of decay, and is defined as the activity per unit mass or per unit volume. The higher the specific activity of a radioisotope, the faster it is decaying.

The activity of a radionuclide at time  $t$  may be calculated by:

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$$A = A_0 e^{-0.693t/T_{\text{rad}}}$$

where A is the activity in dps or curies or becquerels,  $A_0$  is the activity at time zero, t is the time at which measured, and  $T_{\text{rad}}$  is the radiological half-life of the radionuclide ( $T_{\text{rad}}$  and t must be in the same units of time). The time when the activity of a sample of radioactivity becomes one-half its original value is the radioactive half-life and is expressed in any suitable unit of time.

**Table D-1. Characteristics of Nuclear Radiations**

| Radiation                        | Rest mass <sup>a</sup>                 | Charge | Typical energy range | Path length <sup>b</sup> |                     | Comments  |
|----------------------------------|--|--------|----------------------|--------------------------|---------------------|---|
|                                  |  |        |                      | Air                      | Solid               |   |
| Alpha ( $\alpha$ )               | 4.00 amu                               | +2     | 4–10 MeV             | 5–10 cm                  | 25–80 $\mu\text{m}$ | Identical to ionized He nucleus                             |
| Negatron ( $\beta^-$ )           | 5.48x10 <sup>-4</sup> amu;<br>0.51 MeV | -1     | 0–4 MeV              | 0–10 m                   | 0–1 cm              | Identical to electron                                       |
| Positron ( $\beta^+$ )           | 5.48x10 <sup>-4</sup> amu;<br>0.51 MeV | +1     | 0–4 MeV              | 0–10 m                   | 0–1 cm              | Identical to electron except for sign of charge             |
| Neutron                          | 1.0086 amu;<br>939.55 MeV              | 0      | 0–15 MeV             | b                        | b                   | Free half-life: 16 minutes                                  |
| X ray (e.m. photon)              | –                                      | 0      | 5 keV–100 keV        | b                        | b                   | Photon from transition of an electron between atomic orbits |
| Gamma ( $\gamma$ ) (e.m. photon) | –                                      | 0      | 10 keV–3 MeV         | b                        | b                   | Photon from nuclear transformation                          |

<sup>a</sup> The rest mass (in amu) has an energy equivalent in MeV that is obtained using the equation  $E=mc^2$ , where 1 amu = 932 MeV.

<sup>b</sup> Path lengths are not applicable to x- and gamma rays since their intensities decrease exponentially; path lengths in solid tissue are variable, depending on particle energy, electron density of material, and other factors.

amu = atomic mass unit; e.m. = electromagnetic; MeV = MegaElectron Volts

The specific activity is a measure of activity, and is fined as the activity per unit mass or per unit volume. This activity is usually expressed in curies per gram and may be calculated by

$$\text{curies/gram} = 1.3 \times 10^8 / (T_{\text{rad}}) (\text{atomic weight}) \quad \text{or}$$

$$[3.577 \times 10^5 \times \text{mass(g)}] / [T_{\text{rad}} \times \text{atomic weight}]$$

where  $T_{\text{rad}}$  is the radiological half-life in days.

In the case of radioactive materials contained in living organisms, an additional consideration is made for the reduction in observed activity due to regular processes of elimination of the respective chemical or biochemical substance from the organism. This introduces a rate constant called the biological half-life

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( $T_{\text{biol}}$ ) which is the time required for biological processes to eliminate one-half of the activity. This time is virtually the same for both stable and radioactive isotopes of any given element.

Under such conditions the time required for a radioactive element to be halved as a result of the combined action of radioactive decay and biological elimination is the effective clearance half-time:

$$T_{\text{eff}} = (T_{\text{biol}} \times T_{\text{rad}}) / (T_{\text{biol}} + T_{\text{rad}}).$$

Table D-2 presents representative effective half-lives of particular interest.

**Table D-2. Half-Lives of Some Radionuclides in Adult Body Organs**

| Radionuclide                         | Critical organ | Half-life <sup>a</sup> |            |           |
|--------------------------------------|----------------|------------------------|------------|-----------|
|                                      |                | Physical               | Biological | Effective |
| Uranium 238                          | Kidney         | 4,460,000,000 y        | 4 d        | 4 d       |
| Hydrogen 3 <sup>b</sup><br>(Tritium) | Whole body     | 12.3 y                 | 10 d       | 10 d      |
| Iodine 131                           | Thyroid        | 8 d                    | 80 d       | 7.3 d     |
| Strontium 90                         | Bone           | 28 y                   | 50 y       | 18 y      |
| Plutonium 239                        | Bone surface   | 24,400 y               | 50 y       | 50 y      |
|                                      | Lung           | 24,400 y               | 500 d      | 500 d     |
| Cobalt 60                            | Whole body     | 5.3 y                  | 99.5 d     | 95 d      |
| Iron 55                              | Spleen         | 2.7 y                  | 600 d      | 388 d     |
| Iron 59                              | Spleen         | 45.1 d                 | 600 d      | 42 d      |
| Manganese 54                         | Liver          | 303 d                  | 25 d       | 23 d      |
| Cesium 137                           | Whole body     | 30 y                   | 70 d       | 70 d      |

<sup>a</sup>d = days, y = years

<sup>b</sup>Mixed in body water as tritiated water

### D.2.3 Interaction of Radiation with Matter

Both ionizing and nonionizing radiation will interact with materials; that is, radiation will lose kinetic energy to any solid, liquid or gas through which it passes by a variety of mechanisms. The transfer of energy to a medium by either electromagnetic or particulate radiation may be sufficient to cause formation of ions. This process is called ionization. Compared to other types of radiation that may be absorbed, such as ultraviolet radiation, ionizing radiation deposits a relatively large amount of energy into a small volume.

The method by which incident radiation interacts with the medium to cause ionization may be direct or indirect. Electromagnetic radiations (x rays and gamma photons) are indirectly ionizing; that is, they give up their energy in various interactions with cellular molecules, and the energy is then utilized to produce a fast-moving charged particle such as an electron. It is the electron that then may react with a target molecule. This particle is called a “primary ionizing particle. Charged particles, in contrast, strike the tissue or medium and directly react with target molecules, such as oxygen or water. These particulate radiations are directly ionizing radiations. Examples of directly ionizing particles include alpha and beta particles. Indirectly ionizing radiations are always more penetrating than directly ionizing particulate radiations.

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Mass, charge, and velocity of a particle all affect the rate at which ionization occurs. The higher the charge of the particle and the lower the velocity, the greater the propensity to cause ionization. Heavy, highly charged particles, such as alpha particles, lose energy rapidly with distance and, therefore, do not penetrate deeply. The result of these interaction processes is a gradual slowing down of any incident particle until it is brought to rest or "stopped" at the end of its range.

## D.2.4 Characteristics of Emitted Radiation

**D.2.4.1 Alpha Emission.** In alpha emission, an alpha particle consisting of two protons and two neutrons is emitted with a resulting decrease in the atomic mass number by four and reduction of the atomic number of two, thereby changing the parent to a different element. The alpha particle is identical to a helium nucleus consisting of two neutrons and two protons. It results from the radioactive decay of some heavy elements such as uranium, plutonium, radium, thorium, and radon. All alpha particles emitted by a given radioisotope have the same energy. Most of the alpha particles that are likely to be found have energies in the range of about 4 to 8 MeV, depending on the isotope from which they came.

The alpha particle has an electrical charge of +2. Because of this double positive charge and their size, alpha particles have great ionizing power and, thus, lose their kinetic energy quickly. This results in very little penetrating power. In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle (the distance the charged particle travels from the point of origin to its resting point) is about 4 cm in air, which decreases considerably to a few micrometers in tissue. These properties cause alpha emitters to be hazardous only if there is internal contamination (i.e., if the radionuclide is inside the body).

**D.2.4.2 Beta Emission.** A beta particle ( $\beta$ ) is a high-velocity electron ejected from a disintegrating nucleus. The particle may be either a negatively charged electron, termed a negatron ( $\beta^-$ ) or a positively charged electron, termed a positron ( $\beta^+$ ). Although the precise definition of "beta emission" refers to both  $\beta^-$  and  $\beta^+$ , common usage of the term generally applies only to the negative particle, as distinguished from the positron emission, which refers to the  $\beta^+$  particle.

**D.2.4.2.1 Beta Negative Emission.** Beta particle ( $\beta^-$ ) emission is another process by which a radionuclide, with a neutron excess achieves stability. Beta particle emission decreases the number of neutrons by one and increases the number of protons by one, while the atomic mass number remains unchanged.<sup>1</sup> This transformation results in the formation of a different element. The energy spectrum of beta particle emission ranges from a certain maximum down to zero with the mean energy of the spectrum being about one-third of the maximum. The range in tissue is much less. Beta negative emitting radionuclides can cause injury to the skin and superficial body tissues, but mostly present an internal contamination hazard.

**D.2.4.2.2 Positron Emission.** In cases in which there are too many protons in the nucleus, positron emission may occur. In this case a proton may be thought of as being converted into a neutron, and a positron ( $\beta^+$ ) is emitted.<sup>1</sup> This increases the number of neutrons by one, decreases the number of protons by one, and again leaves the atomic mass number unchanged. The gamma radiation resulting from the annihilation (see glossary) of the positron makes all positron emitting isotopes more of an external radiation hazard than pure  $\beta$  emitters of equal energy.

**D.2.4.2.3 Gamma Emission.** Radioactive decay by alpha, beta, or positron emission, or electron capture often leaves some of the energy resulting from these changes in the nucleus. As a result, the nucleus is raised to an excited level. None of these excited nuclei can remain in this high-energy state.

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<sup>1</sup> Neutrinos also accompany negative beta particles and positron emissions

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Nuclei release this energy returning to ground state or to the lowest possible stable energy level. The energy released is in the form of gamma radiation (high energy photons) and has an energy equal to the change in the energy state of the nucleus. Gamma and x rays behave similarly but differ in their origin; gamma emissions originate in the nucleus while x rays originate in the orbital electron structure or from rapidly changing the velocity of an electron (e.g., as occurs when shielding high energy beta particles or stopping the electron beam in an x ray tube).

### D.3 ESTIMATION OF ENERGY DEPOSITION IN HUMAN TISSUES

Two forms of potential radiation exposures can result: internal and external. The term exposure denotes physical interaction of the radiation emitted from the radioactive material with cells and tissues of the human body. An exposure can be "acute" or "chronic" depending on how long an individual or organ is exposed to the radiation. Internal exposures occur when radionuclides, which have entered the body (e.g., through the inhalation, ingestion, or dermal pathways), undergo radioactive decay resulting in the deposition of energy to internal organs. External exposures occur when radiation enters the body directly from sources located outside the body, such as radiation emitters from radionuclides on ground surfaces, dissolved in water, or dispersed in the air. In general, external exposures are from material emitting gamma radiation, which readily penetrate the skin and internal organs. Beta and alpha radiation from external sources are far less penetrating and deposit their energy primarily on the skin's outer layer. Consequently, their contribution to the absorbed dose of the total body dose, compared to that deposited by gamma rays, may be negligible.

Characterizing the radiation dose to persons as a result of exposure to radiation is a complex issue. It is difficult to: (1) measure internally the amount of energy actually transferred to an organic material and to correlate any observed effects with this energy deposition; and (2) account for and predict secondary processes, such as collision effects or biologically triggered effects, that are an indirect consequence of the primary interaction event.

#### D.3.1 Dose/Exposure Units

**D.3.1.1 Roentgen.** The roentgen (R) is a unit of x or gamma-ray exposure and is measured by the amount of ionization caused in air by gamma or x radiation. One roentgen produces  $2.58 \times 10^{-4}$  coulomb per kilogram of air. In the case of gamma radiation, over the commonly encountered range of photon energy, the energy deposition in tissue for a dose of 1 R is about 0.0096 joules (J) /kg of tissue.

**D.3.1.2 Absorbed Dose and Absorbed Dose Rate.** The absorbed dose is defined as the energy imparted by the incident radiation to a unit mass of the tissue or organ. The unit of absorbed dose is the rad; 1 rad = 100 erg/gram = 0.01 J/kg in any medium. An exposure of 1 R results in a dose to soft tissue of approximately 0.01 J/kg. The SI unit is the gray which is equivalent to 100 rad or 1 J/kg. Internal and external exposures from radiation sources are not usually instantaneous but are distributed over extended periods of time. The resulting rate of change of the absorbed dose to a small volume of mass is referred to as the absorbed dose rate in units of rad/unit time.

**D.3.1.3 Working Levels and Working Level Months.** Working level (WL) is a measure of the atmospheric concentration of radon and its short-lived progeny. One WL is defined as any combination of short-lived radon daughters (through polonium-214), per liter of air, that will result in the emission of  $1.3 \times 10^5$  MeV of alpha energy. An activity concentration of 100 pCi radon-222/L of air, in equilibrium with its daughters, corresponds approximately to a potential alpha-energy concentration of 1 WL. The WL unit can also be used for thoron daughters. In this case,  $1.3 \times 10^5$  MeV of alpha energy (1 WL) is released by the thoron daughters in equilibrium with 7.5 pCi thoron/L. The potential alpha energy exposure of miners is commonly expressed in the unit Working Level Month (WLM). One WLM

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corresponds to exposure to a concentration of 1 WL for the reference period of 170 hours, or more generally

$$\text{WLM} = \text{concentration (WL)} \times \text{exposure time (months)} \quad (\text{one "month"} = 170 \text{ working hours}).$$

### D.3.2 Dosimetry Models

Dosimetry models are used to estimate the dose from internally deposited radioactive substances. The models for internal dosimetry consider the amount of radionuclides entering the body, the factors affecting their movement or transport through the body, distribution and retention of radionuclides in the body, and the energy deposited in organs and tissues from the radiation that is emitted during spontaneous decay processes. The dose pattern for radioactive materials in the body may be strongly influenced by the route of entry of the material. For industrial workers, inhalation of radioactive particles with pulmonary deposition and puncture wounds with subcutaneous deposition have been the most frequent. The general population has been exposed via ingestion and inhalation of low levels of naturally occurring radionuclides as well as radionuclides from nuclear weapons testing.

The models for external dosimetry consider only the photon doses to organs of individuals who are immersed in air or are exposed to a contaminated object.

**D.3.2.1 Ingestion.** Ingestion of radioactive materials is most likely to occur from contaminated foodstuffs or water or eventual ingestion of inhaled compounds initially deposited in the lung. Ingestion of radioactive material may result in toxic effects as a result of either absorption of the radionuclide or irradiation of the gastrointestinal tract during passage through the tract, or a combination of both. The fraction of a radioactive material absorbed from the gastrointestinal tract is variable, depending on the specific element, the physical and chemical form of the material ingested, and the diet, as well as some other metabolic and physiological factors. The absorption of some elements is influenced by age, usually with higher absorption in the very young.

**D.3.2.2 Inhalation.** The inhalation route of exposure has long been recognized as being a major portal of entry for both nonradioactive and radioactive materials. The deposition of particles within the lung is largely dependent upon the size of the particles being inhaled. After the particle is deposited, the retention will depend upon the physical and chemical properties of the dust and the physiological status of the lung. The retention of the particle in the lung depends on the location of deposition, in addition to the physical and chemical properties of the particles. The converse of pulmonary retention is pulmonary clearance. There are three distinct mechanisms of clearance which operate simultaneously. Ciliary clearance acts only in the upper respiratory tract. The second and third mechanisms act mainly in the deep respiratory tract. These are phagocytosis and absorption. Phagocytosis is the engulfing of foreign bodies by alveolar macrophages and their subsequent removal either up the ciliary "escalator" or by entrance into the lymphatic system. Some inhaled soluble particles are absorbed into the blood and translocated to other organs and tissues.

### D.3.3 Internal Emitters

An internal emitter is a radionuclide that is inside the body. The absorbed dose from internally deposited radioisotopes depends on the energy absorbed per unit tissue by the irradiated tissue. For a radioisotope distributed uniformly throughout an infinitely large medium, the concentration of absorbed energy must be equal to the concentration of energy emitted by the isotope. An infinitely large medium may be approximated by a tissue mass whose dimensions exceed the range of the particle. All alpha and most beta radiation will be absorbed in the organ (or tissue) of reference. Gamma-emitting isotope emissions are penetrating radiation, and a substantial fraction of gamma energy may be absorbed in tissue. The dose

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to an organ or tissue is a function of the effective retention half-time, the energy released in the tissue, the amount of radioactivity initially introduced, and the mass of the organ or tissue.

## D.4 BIOLOGICAL EFFECTS OF RADIATION

When biological material is exposed to ionizing radiation, a chain of cellular events occurs as the ionizing particle passes through the biological material. A number of theories have been proposed to describe the interaction of radiation with biologically important molecules in cells and to explain the resulting damage to biological systems from those interactions. Many factors may modify the response of a living organism to a given dose of radiation. Factors related to the exposure include the dose rate, the energy of the radiation, and the temporal pattern of the exposure. Biological considerations include factors such as species, age, sex, and the portion of the body exposed. Several excellent reviews of the biological effects of radiation have been published, and the reader is referred to these for a more in-depth discussion (Brodsky 1996; Hobbs and McClellan 1986; ICRP 1984; Mettler and Moseley 1985; Rubin and Casarett 1968).

### D.4.1 Radiation Effects at the Cellular Level

According to Mettler and Moseley (1985), at acute doses up to 10 rad (100 mGy), single strand breaks in DNA may be produced. These single strand breaks may be repaired rapidly. With doses in the range of 50–500 rad (0.5–5 Gy), irreparable double-stranded DNA breaks are likely, resulting in cellular reproductive death after one or more divisions of the irradiated parent cell. At large doses of radiation, usually greater than 500 rad (5 Gy), direct cell death before division (interphase death) may occur from the direct interaction of free-radicals with essentially cellular macromolecules. Morphological changes at the cellular level, the severity of which are dose-dependent, may also be observed.

The sensitivity of various cell types varies. According to the Bergonie-Tribondeau law, the sensitivity of cell lines is directly proportional to their mitotic rate and inversely proportional to the degree of differentiation (Mettler and Moseley 1985). Rubin and Casarett (1968) devised a classification system that categorized cells according to type, function, and mitotic activity. The categories range from the most sensitive type, "vegetative intermitotic cells," found in the stem cells of the bone marrow and the gastrointestinal tract, to the least sensitive cell type, "fixed postmitotic cells," found in striated muscles or long-lived neural tissues.

Cellular changes may result in cell death, which if extensive, may produce irreversible damage to an organ or tissue or may result in the death of the individual. If the cell recovers, altered metabolism and function may still occur, which may be repaired or may result in the manifestation of clinical symptoms. These changes may also be expressed at a later time as tumors or cellular mutations, which may result in abnormal tissue.

### D.4.2 Radiation Effects at the Organ Level

In most organs and tissues the injury and the underlying mechanism for that injury are complex and may involve a combination of events. The extent and severity of this tissue injury are dependent upon the radiosensitivity of the various cell types in that organ system. Rubin and Casarett (1968) describe and schematically display the events following radiation in several organ system types. These include: a rapid renewal system, such as the gastrointestinal mucosa; a slow renewal system, such as the pulmonary epithelium; and a nonrenewal system, such as neural or muscle tissue. In the rapid renewal system, organ injury results from the direct destruction of highly radiosensitive cells, such as the stem cells in the bone marrow. Injury may also result from constriction of the microcirculation and from edema and inflammation of the basement membrane, designated as the histohematic barrier (HHB), which may



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progress to fibrosis. In slow renewal and nonrenewal systems, the radiation may have little effect on the parenchymal cells, but ultimate parenchymal atrophy and death over several months result from HHB fibrosis and occlusion of the microcirculation.

#### **D.4.3 Low Level Radiation Effects**

Cancer is the major latent harmful effect produced by ionizing radiation and the one that most people exposed to radiation are concerned about. The ability of alpha, beta, and gamma radiation to produce cancer in virtually every tissue and organ in laboratory animals has been well-demonstrated. The development of cancer is not an immediate effect. Radiation-induced leukemia has the shortest latent period at 2 years, while other radiation induced cancers have latent periods >20 years. The mechanism by which cancer is induced in living cells is complex and is a topic of intense study. Exposure to ionizing radiation can produce cancer at any site within the body; however, some sites appear to be more common than others, such as the breast, lung, stomach, and thyroid.

DNA is a major target molecule during exposure to ionizing radiation. Other macromolecules, such as lipids and proteins, are also at risk of damage when exposed to ionizing radiation. The genotoxicity of ionizing radiation is an area of intense study, as damage to the DNA is ultimately responsible for many of the adverse toxicological effects ascribed to ionizing radiation, including cancer. Damage to genetic material is basic to developmental or teratogenic effects, as well. However, for effects other than cancer, there is little evidence of human effects at low levels of exposure.

### **D.5 UNITS IN RADIATION PROTECTION AND REGULATION**

#### **D.5.1 Dose Equivalent and Dose Equivalent Rate**

Dose equivalent or rem is a special radiation protection quantity that is used, for administrative and radiation safety purposes only, to express the absorbed dose in a manner which considers the difference in biological effectiveness of various kinds of ionizing radiation. The ICRU has defined the dose equivalent,  $H$ , as the product of the absorbed dose,  $D$ , and the quality factor,  $Q$ , at the point of interest in biological tissue. This relationship is expressed as  $H = D \times Q$ . The dose equivalent concept is applicable only to doses that are not great enough to produce biomedical effects.

The quality factor is a dimensionless quantity that depends in part on the stopping power for charged particles, and it accounts for the differences in biological effectiveness found among the types of radiation. Originally relative biological effectiveness (RBE) was used rather than  $Q$  to define the quantity, rem, which was of use in risk assessment. The generally accepted values for quality factors for various radiation types are provided in Table D-3. The dose equivalent rate is the time rate of change of the dose equivalent to organs and tissues and is expressed as rem/unit time or sievert/unit time.

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**Table D-3. Quality Factors (Q) and Absorbed Dose Equivalencies**

| Type of radiation  | Quality factor (Q) | Absorbed dose equal to a unit dose equivalent* |
|--|--------------------|--|
| X, gamma, or beta radiation  | 1                  | 1  |
| Alpha particles, multiple-charged particles, fission fragments and heavy particles of unknown charge | 20                 | 0.05   |
| Neutrons of unknown energy   | 10                 | 0.1  |
| High-energy protons  | 10                 | 0.1  |

\*Absorbed dose in rad equal to 1 rem or the absorbed dose in gray equal to 1 sievert.

Source: USNRC. 1999. Standards for the protection against radiation, table 1004(b).1. 10 CFR 20.1004. U.S. Nuclear Regulatory Commission, Washington, D.C.

### D.5.2 Relative Biological Effectiveness

RBE is used to denote the experimentally determined ratio of the absorbed dose from one radiation type to the absorbed dose of a reference radiation required to produce an identical biologic effect under the same conditions. Gamma rays from cobalt-60 and 200–250 keV x-rays have been used as reference standards. The term RBE has been widely used in experimental radiobiology, and the term quality factor used in calculations of dose equivalents for radiation safety purposes (ICRP 1977; NCRP 1971; UNSCEAR 1982). RBE applies only to a specific biological end point, in a specific exposure, under specific conditions to a specific species. There are no generally accepted values of RBE.

### D.5.3 Effective Dose Equivalent and Effective Dose Equivalent Rate

The absorbed dose is usually defined as the mean absorbed dose within an organ or tissue. This represents a simplification of the actual problem. Normally when an individual ingests or inhales a radionuclide or is exposed to external radiation that enters the body (gamma), the dose is not uniform throughout the whole body. The simplifying assumption is that the detriment will be the same whether the body is uniformly or non-uniformly irradiated. In an attempt to compare detriment from absorbed dose of a limited portion of the body with the detriment from total body dose, the ICRP (1977) has derived a concept of effective dose equivalent. The effective dose equivalent,  $H_E$ , is

$$H_E = (\text{the sum of}) W_t H_t$$

where  $H_t$  is the dose equivalent in the tissue,  $W_t$  is the weighting factor, which represents the estimated proportion of the stochastic risk resulting from tissue, T, to the stochastic risk when the whole body is uniformly irradiated for occupational exposures under certain conditions (ICRP 1977). Weighting factors for selected tissues are listed in Table D-4.

The ICRU (1980), ICRP (1984), and NCRP (1985) now recommend that the rad, roentgen, curie, and rem be replaced by the SI units: gray (Gy), Coulomb per kilogram (C/kg), Becquerel (Bq), and sievert (Sv), respectively. The relationship between the customary units and the international system of units (SI) for radiological quantities is shown in Table D-5.

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**Table D-4. Weighting Factors for Calculating Effective Dose Equivalent for Selected Tissues**

| Tissue       | Weighting factor |                 |      |
|--------------|------------------|-----------------|------|
|              | ICRP60           | NCRP115/ ICRP60 | NRC  |
| Bladder      | 0.040            | 0.05            | –    |
| Bone marrow  | 0.143            | 0.12            | 0.12 |
| Bone surface | 0.009            | 0.01            | 0.03 |
| Breast       | 0.050            | 0.05            | 0.15 |
| Colon        | 0.141            | 0.12            | –    |
| Liver        | 0.022            | 0.05            | –    |
| Lung         | 0.111            | 0.12            | 0.12 |
| Esophagus    | 0.034            | 0.05            | –    |
| Ovary        | 0.020            | 0.05            | –    |
| Skin         | 0.006            | 0.01            | –    |
| Stomach      | 0.139            | 0.12            | –    |
| Thyroid      | 0.021            | 0.05            | 0.03 |
| Gonads       | 0.183            | 0.20            | 0.25 |
| subtotal     | 0.969            | 1               | 0.70 |
| Remainder    | 0.031            | 0.05            | 0.30 |

ICRP60 = International Commission on Radiological Protection, 1990 Recommendations of the ICRP  
 NCRP115 = National Council on Radiation Protection and Measurements. 1993. Risk Estimates for Radiation Protection, Report 115. Bethesda, Maryland  
 NRC = Nuclear Regulatory Commission, Title 10, Code of Federal Regulations, Part 20

**Table D-5. Comparison of Common and SI Units for Radiation Quantities**

| Quantity                           | Customary units   | Definition   | SI units  | Definition                               |
|------------------------------------|---|--|---|--|
| Activity (A)                       | curie (Ci)  | $3.7 \times 10^{10}$ transformations s <sup>-1</sup> | becquerel (Bq)  | s <sup>-1</sup>                          |
| Absorbed dose (D)                  | rad (rad)   | $10^{-2}$ Jkg <sup>-1</sup>                          | gray (Gy)   | Jkg <sup>-1</sup>                        |
| Absorbed dose rate ( $\dot{D}$ )   | rad per second (rad s <sup>-1</sup> )                       | $10^{-2}$ Jkg <sup>-1</sup> s <sup>-1</sup>          | gray per second (Gy s <sup>-1</sup> )                       | Jkg <sup>-1</sup> s <sup>-1</sup>        |
| Dose equivalent (H)                | rem (rem)   | $10^{-2}$ Jkg <sup>-1</sup>                          | sievert (Sv)  | Jkg <sup>-1</sup>                        |
| Dose equivalent rate ( $\dot{H}$ ) | rem per second (rem s <sup>-1</sup> )                       | $10^{-2}$ Jkg <sup>-1</sup> s <sup>-1</sup>          | sievert per second (Sv s <sup>-1</sup> )                    | Jkg <sup>-1</sup> s <sup>-1</sup>        |
| Linear energy transfer (LET)       | kiloelectron volts per micrometer (keV $\mu\text{m}^{-1}$ ) | $1.602 \times 10^{-10}$ Jm <sup>-1</sup>             | kiloelectron volts per micrometer (keV $\mu\text{m}^{-1}$ ) | $1.602 \times 10^{-10}$ Jm <sup>-1</sup> |

Jkg<sup>-1</sup> = Joules per kilogram; Jkg<sup>-1</sup>s<sup>-1</sup> = Joules per kilogram per second; Jm<sup>-1</sup> = Joules per meter; s<sup>-1</sup> = per second

## APPENDIX D

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